## REMARKS

Claims 77-82 are pending and under active consideration.

Claim 77 has been amended to recite the full name of the depository ("Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH") in which the 8F4 antibody is deposited.

The amendments to the specification made in the Response to Restriction Requirement with Preliminary Amendment Under 37 C.F.R. § 1.115 dated September 7, 2006 are reintroduced herein, referring to page and paragraph number of the application as filed instead of the patent publication of the above-identified application.

The Abstract has been amended to place references to "said 8F4" molecule to "the 8F4 molecule."

No new matter is introduced by the amendments made herein.

## OBJECTIONS TO PRIOR AMENDMENTS TO THE SPECIFICATION

In paragraph 5 of the Office Action, the Examiner indicated that the amendments made to the specification in the Response to Restriction Requirement with Preliminary Amendment Under 37 C.F.R. § 1.115 dated September 7, 2006 have not been entered because they refer to paragraphs in the patent publication instead of the patent application.

The amendments are reintroduced herein, referring to page and paragraph number of the application as filed instead of the patent publication of the above-identified application. Entry of the amendments is requested.

## THE OBJECTION TO THE ABSTRACT SHOULD BE WITHDRAWN

In paragraph 8 of the Office Action, the Examiner objected to the Abstract for use of legal phraseology such as "said." In response, Applicant has amended the Abstract to delete legal terminology. It is requested that the objection to the Abstract be withdrawn.

## INFORMATION DISCLOSURE STATEMENT

The Examiner has indicated that certain references cited in the Information Disclosure Statement filed on October 24, 2005, which Applicant stated were provided in the file of parent application no. 09/509,283, could not be located in the file of the parent application. At the request of the Examiner, these references, which were lined through by the Examiner

and believed to be references B02-B06; C01-C13; C15-C22; C24; C26-C35; and C37, are being submitted concurrently herewith.

## THE OBJECTION TO CLAIM 77 SHOULD BE WITHDRAWN

Claim 77 is objected to because it contains the first occurrence of the abbreviation "DSMZ" in the claims without being accompanied by the full name of the depository. In response, Applicant has amended claim 77 has been amended to recite the full name of the depository ("Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH"). Accordingly, it is requested that the objection be withdrawn.

## THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

The Examiner has rejected the claims under 35 U.S.C. § 112, first paragraph, for lack of enablement. In particular, the Examiner contends that "the specification, while being enabling for a method of treating an asthmatic disorder, and a method of treating an organ transplant rejection, does not reasonably provide enablement for a method of treating a generically recited 'immune disorder' or 'autoimmune disorder'."

Applicant respectfully disagrees. According to applicable case law, an invention is enabled even though the disclosure may require some routine experimentation to practice the invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). A considerable amount of experimentation is permitted if it is merely routine or the specification provides reasonable amount of guidance and direction to the experimentation. *In re Jackson*, 217 U.S.P.Q. 804, 807 (1982). Where a disclosure provides direction and guidance on how to practice the invention and where, at the time of application, the skill in the art was quite high and the methods needed to practice the invention well known, a conclusion of enablement should be made. *In re Wands*, 858 F.2d 731, 740, 8 U.S.P.Q.2d. 1400, 1406 (Fed. Cir. 1988). Applicant submit that the skill in the respective fields of molecular biology, immunology and biochemistry was very high, and that general methods for antibody testing and optimization were well known, as of the September 1997 priority date of the instant application. Accordingly, Applicant submits that the specification as filed provides sufficient support under § 112 for methods of use of anti-ICOS antibodies to treat immune diseases and autoimmune diseases.

The Examiner's remaining assertions do not explain why one skilled in the art would not know how to make or use the invention. Rather, the Examiner alleges that it is unpredictable whether the claimed methods would work for the treatment of a genus of immune and autoimmune diseases. Applicant respectfully points out that the basis of the Examiner's rejection is alleged lack of utility applied under § 112, rather than lack of enablement.

The Utility Guidelines (M.P.E.P. 706.03(a)(1)) are applicable when there is an allegation of lack of utility under § 112. Under the Utility Guidelines, evidence of utility is sufficient if it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. All that is required is a reasonable correlation between the effectiveness of the methods and the asserted use. (See Utility Guidelines, M.P.E.P. 706.03(a)(1))

In particular, the Examiner's assertions that animal models of pharmaceutical therapies in the absence of *in vivo* data are unpredictable and that antibody therapeutics are not sufficiently predictive of the utility of the presently claimed invention are unfounded, both from a legal viewpoint and a scientific viewpoint.

From a legal perspective, the Federal Circuit in *In re Brana* (51 F.3d 1560, 34 USPQ2d 1436, Fed. Cir. 1995) held that test results showing antitumor activity of compounds against a standard tumor model *in vivo* are acceptable as evidence of utility sufficient to meet the requirement of 35 U.S.C. § 112, first paragraph. As explained in *In re Brana*, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995), the USPTO should not confuse "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption," citing *Scott v. Finney*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994). Moreover, section 112 does not require that optimal efficacy be provided by the invention, merely that some efficacy be provided. See MPEP 2164.08 (3)(b) and *Ex parte Ferguson*, 117 U.S.P.Q. 229 (Bd. App. 1957).

From the scientific viewpoint, the Examiner's attention is directed to the accompanying Declaration Under 37 C.F. R. § 1.132 by inventor Richard Kroczek, M.D. ("Kroczek Declaration"). The Kroczek Declaration provides an overview of post-filing date literature that provides evidence of ICOS's general role in immune and autoimmune disorders, which in addition to asthma and organ transplant rejection include inflammatory bowel disease, systemic lupus erythomatosus, autoimmune myocarditis, myasthenia gravis,

multiple sclerosis and rheumatoid arthritis. Dr. Kroczek concludes that:

> The studies described herein implicate ICOS in a wide spectrum of immune and autoimmune diseases. The animal models of disease employed in the studies are the best approximations of the corresponding human diseases known to the scientific community and are used by the pharmaceutical industry in preclinical studies of clinical candidates. The data obtained from the studies described above strongly indicate that treatment of a number of such diseases can be achieved by inhibiting the ICOS pathway, for example by use of an anti-ICOS antibody. Indeed, on the basis of studies such as those described herein, MedImmune Inc. has licensed an anti-ICOS antibody from Japan Tobacco Inc. for development as an anti-inflammatory therapeutic for autoimmune disorders SLE and RA (see, *e.g.*, Exhibit 22, Bioworld Today December 29, 2006 at pages 1-2). It is also my opinion that most, if not all, inhibitory anti-ICOS antibodies will exhibit some efficacy towards treatment of such diseases, and that optimization of any given antibody for clinical use (*e.g.*, by chimerization or humanization and/or improvement of the binding kinetics by mutagenesis of the antibodies' complementarity determining regions) could have been performed as of September 1997 using standard methodologies.

Kroczek Declaration at paragraph 41.

Applicant submits that the Kroczek Declaration provides evidence that inhibiting the ICOS pathway, for example by the use of anti-ICOS antibodies, results in the amelioration of the symptoms of many immune and autoimmune diseases in a number of art-recognized animal models, which are the best approximations of the corresponding human disorders and are used in preclinical studies of clinical candidates. Thus the legal standard for § 112, first paragraph, namely that the invention has some efficacy, is fulfilled by the presently claimed invention.

In view of the foregoing, Applicant requests that rejection of the claims under § 112, first paragraph be withdrawn.

## THE DOUBLE PATENTING REJECTION

The presently pending claims are rejected on the grounds of obviousness-type double patenting over claims 1-5 of U.S. Patent No. 7,125,551. In addition, the claims are provisionally rejected on the grounds of obviousness-type double patenting over claims 21-35 of U.S. Application No. 09/823,307.

Applicant respectfully requests that the rejection be held in abeyance until such time an indication is made that the claims are allowable but for a terminal disclaimer. Without agreeing with the rejection, Applicant will submit a terminal disclaimer over U.S. Patent No.

7,125,551 and the patent issuing on U.S. Application No. 09/823,307 at such time that an indication is made that the claims are allowable but for a terminal disclaimer.

## CONCLUSION

Applicant respectfully requests that the amendments and remarks made herein be entered and made of record in the file history of the subject application. It is submitted that the application is in condition for allowance. An allowance is earnestly requested.

Respectfully submitted,

Date: May 2, 2007

Nikolaos C. George 39,201
Nikolaos C. George (Reg. No.)

**JONES DAY**
222 East 41st Street
New York, New York 10017
(212) 326-3939

by: Mina Abu-Shaar
L0012